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TITLE: "A Civilian/Military Trauma Institute: National Trauma Coordinating Center"

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CONTRACTING ORGANIZATION:
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**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**
The purpose of this grant is to support a national coordinating center for trauma research funding. The infrastructure/process is streamlined and efficient leading to the selection of research projects based on a solid scientific, peer review of submitted research proposals. Three of the four selected research projects are complete and the fourth is well on its way to achieving the objective.

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## INTRODUCTION

The University of Texas Health Science Center at San Antonio (UTHSCSA) proposed to utilize $2,101,000 in congressional funding to work collaboratively with National Trauma Institute (NTI) to build on the establishment of NTI as a national coordinating center for trauma research funding. In addition, a forum for dissemination of trauma research information was provided for the trauma community through the NTI Annual Trauma Conference. One year no-cost extensions were approved in September 2011 and 2012. A 24 month no-cost extension was approved September 2013. A final one year no-cost extension was requested in June of 2015, has been approved by the COR and execution of award modification remains pending. This final year will allow for the last research study to complete enrollment.

## Body

### Statement of Work

A. The contractor will support a national coordinating center for trauma research funding.

1. Requests for proposals (RFP) based on areas of scientific merit in trauma and emergency or critical care will be prepared and issued.
2. NTI Board Science Committee will score proposals according to scientific merit, clinical impact and ability to perform.
3. NTI Board will update trauma research subject areas based upon the basis of impact on survival or care of patients, existing funding, and funding availability annually.
4. Perform Award management and compliance to include all appropriate USAMRMC HRPO requirements.
5. Provide research funding for proposals that seek to address areas of urgent need in the treatment of trauma.
    a) Timing and Mechanism of Traumatic Coagulopathy, PI - Mitchell Cohen, MD, University of California, San Francisco.
    b) Comparative Effectiveness of Clinical Care Processes in Resuscitation and Management of Moderate to Severe Traumatic Injuries. PI - Shahid Shafi, MPH, MD, FACS, Baylor Research Institute
    c) Characterization of the Effects of Early Sex-Hormone Environment Following Injury, PI - Jason L. Sperry, MD, MPH, University of Pittsburgh
    d) Vasopressin Supplementation during the Resuscitation of Hemorrhagic Shock PI - Carrie Sims, MD, MS, University of Pennsylvania

B. The contractor will provide a forum for dissemination of trauma research information to the trauma community.

**A. National Coordinating Center for Trauma Research Funding:**

**Research Funding For Proposals that Address Areas of Urgent Need in the Treatment of Trauma**

**Project 1:**

Project Title: Vasopressin Supplementation during the Resuscitation of Hemorrhagic Shock
PI Name: Carrie Sims, MD, MS

PI Institution: University of Pennsylvania
Status: HRPO Log# A-16375.4, approved 12/31/12.

**Current Progress:**

This project utilizes the Exception from Informed Consent and Community Consultation (10USC980). The project was reviewed and approved by the Secretary of the Army. Contracting was complete and study was initiated.

Enrollment began on 5/16/13. Over the past year, screening and enrollment of eligible subjects has continued. As of the investigators last report there have been 70 subjects enrolled. The trauma center successfully transitioned to Pennsylvania Presbyterian Medical Center in February 2015and there have been no issues with randomization or obtaining the study drug from Investigational Drug Services. In October of 2014 the PI requested IRB approval to draw an additional two tablespoons of blood to evaluate coagulation parameters including platelet function and peripheral mononuclear cell function. These new procedures would allow the research team to see how blood is clotting and how cells are fighting off infection. This amendment was approved by the University of Pennsylvania IRB on 11/20/2014 and submitted to HRPO on 12/1/2014. Subsequently HRPO determined the proposed amendments are not substantive or modifications that could potentially increase risk to subjects and their approval prior to implementation was not required but could be submitted with the next continuing review. .

An interim analysis of 50 subjects was completed and although there was a significant difference on univariate analysis this did not hold up on multivariate. While the total number of adverse events and serious events was not statistically higher in one group, the incidence of deep venous thrombosis (DVT) was statistically different. A DSMB meeting was convened in May of 2015 and the data were discussed. The DSMB concluded that given the low total number of enrolled subjects the lack of statistical difference on multivariate analysis may be related to an underpowered sample size. It was recommended that the study proceed with enrollment. In terms of potential complications, the DSMB was concerned and wanted further detail regarding the circumstances and timing surrounding the diagnosis of DVT. Of the total 14 DVT's, 7 were associated with direct trauma to the limb developing the DVT. Of the remaining 7 DVT events, 2 occurred within 5 days post trauma, whereas 5 occurred between the $6^{th}$ and $30^{th}$ day post trauma. An interim analysis will be completed after 75 subjects have been enrolled.

**Completed Projects:**

**Research Project 2:**

Project Title: Comparative Effectiveness of Clinical Care Processes in Resuscitation and Management of Moderate to Severe Traumatic Injuries
PI Name: Shahid Shafi, MPH, MD, FACS
Participating sites: Baylor Research Institute (lead), the University of Texas Health Science Center-Houston, University of California, Los Angeles, and Massachusetts General Hospital in Boston.
**Details:** This project's period of performance ended on 12/31/12. Final report summary was included on year 3 annual report dated 10/23/13.

**Research Project 3:**

Project Title: Characterization of the effects of early sex-hormone environment following injury
PI Name: Jason L. Sperry, MD, MPH
Participating site: University of Pittsburgh
**Details:** This project's period of performance was completed on 12/31/12. The project was completed using funding from [contract# W81XWH-11-1-0841] and conclusion was also reported there. The extra funding allowed for increased patient enrollment. The final report summary was included on year 3 annual report dated 10/23/13.

**Research Project 4:**
Project Title: Timing and Mechanism of Traumatic Coagulopathy
PI Name: Mitchell Cohen, MD
Participating sites: University of California, Berkeley (UCSF/San Francisco General Hospital (SFGH) (lead site) and the University of Texas Health Science Center at Houston (UTHSC-Houston), Center for Translational Injury Research (CeTIR).
**Details:** This project's period of performance was completed on 9/24/13. Due to delays in final report submission, the findings are included here.
**Study summary:** Clinically significant platelet dysfunction after trauma exists in the presence of an otherwise reassuring platelet count and clotting studies, with profound implications for mortality. Impedance aggregometry reliably identifies this dysfunction in injured patients, and admission arachidonic acid and collagen responsiveness are significant predictors of both early and late mortality. The significance of low Glasgow Coma Score (GCS) as an independent predictor of platelet hypofunction highlights the importance of further investigation into the link between traumatic brain injury and platelet dysfunction. The clinical availability of rapid, point-of-care platelet function testing will lead to improved triage, more appropriately targeted therapy, and better outcomes after trauma.

**B. Provide a Forum for Dissemination of Research Outcomes to the Trauma Community.**

The 16th National Trauma Institute Annual Symposium was held August 30-September 1, 2010. This task is complete and has been discussed in prior annual reports.

**Table 1: Overall Award Milestones**

| Milestone | Planned Date | Actual Date | Projected Completion Date | Status |
|---|---|---|---|---|
| Grant Awards Announced | Q1 | 3/31/10 | Q1 | Complete |
| Contracting | Q1 | 10/5/2010 | January 2013 | Complete |
| Compliance Management | Q1-ongoing | 10/5/2010 – ongoing | At termination of contract | Ongoing |
| Cost reimbursement | Milestone-based, associated with reporting | | September 2015 | Ongoing |

| Milestone | Planned Date | Actual Date | Projected Completion Date | Status |
|---|---|---|---|---|
| Reporting | Quarterly & Annually | All quarters | September 2015 | Ongoing |
| 2010 Symposium Management/ Organization | 2010 | 2010 | 2010 | Complete |
| Symposium held | August 2010 | 8/31/2010 | 8/31/2010 | Complete |

**Key Research Accomplishments**

None at this time

**Reportable Outcomes**

**Project 1:**

Project Title: Vasopressin Supplementation during the Resuscitation of Hemorrhagic Shock
PI Name: Carrie Sims, MD, MS

1. Smallwood, A. presented the AERT Trial at the 2014 Pennsylvania Committee on Trauma Paper Competition, Harrisburg, PA, October 22-24, 2014. (only medical student selected to present)

2. Sims, C. presented the AVERT Trial in her lecture entitled "Novel Resuscitative Strategies", San Francisco, CA, October, 2014 (recipient of the American College of Surgeons Jacobson Promising Investigator Award)

3. Sims, C. presented the AVERT Trial at the AHA ReSS meeting, Chicago, IL, November, 2014 (pro con debate about vasopressors during the resuscitation of hemorrhagic shock).

4. Maher, Z. Does Proximity to Violence Negatively Influence Attitudes Toward Exception From Informed Consent in Emergency Research? Presented at the Eastern Association for the Surgery of Trauma (EAST) Scientific Assembly, Orlando, FL, January 16, 2015. **(Attachment A)**

5. Maher, Z. AVERT Shock Trial presented at Shock Trauma Surgical Grand Rounds, Rutgers Surgical Grand Rounds, February, 2015.

6. Maher, Z, Grill, EK, Smith, BP, Sims, CA. Does proximity to violence negatively influence attitudes toward exception from informed consent in emergency research? *J Trauma Acute Care Surg*. 2015:79(3):364-371. **(Attachment B)**

**Conclusion**

NTI has successfully completed a RFP, peer-review process, selection of four relevant trauma projects, and is conducting on-going management of the projects under this award.

Three of the four studies funded through this award are complete. Preliminary and final findings of the three completed studies indicate additional research is needed. Each project offers findings that are applicable in today's trauma environment and have the potential to reduce mortality and suggest gender is an important aspect when caring for the trauma patient. The fourth research project continues to evaluate Vasopressin Supplementation during the Resuscitation of Hemorrhagic Shock with the development of targeted interventions to address hemorrhagic shock. This project continues to work towards potential to impact care and change current practices as they relate to coagulation, resuscitation and management of severe traumatic injuries. Each of the funded projects remains of critical importance in the advancement in trauma care.

## Abbreviations

| | |
|---|---|
| AAST | American Association for the Surgery of Trauma |
| CeTIR | Center for Translational Injury Research |
| COR | Contract Officer Representative |
| DSMB | Data Safety Monitoring Board |
| DVT | Deep Vein Thrombosis |
| HRPO | Human Research Protection Office |
| IRB | Institutional Review Board |
| PI | Principal Investigator |
| RFP | Request for Proposal |
| UTHSCSA | University of Texas Health Science Center San Antonio |
| UCLA | University of California Los Angeles |
| UCSF | University of California San Francisco |
| USAMRMC | United States Army Medical and Material Command |

# DOES PROXIMITY TO VIOLENCE NEGATIVELY INFLUENCE ATTITUDES TOWARD EXCEPTION FROM INFORMED CONSENT IN EMERGENCY RESEARCH?

**Introduction**: Exception from Informed Consent (EFIC) presents a challenge to researchers, in part due to concern about patient reluctance to participate. It is unknown what community characteristics affect respondents' attitudes toward EFIC or their willingness to participate in emergency research. We hypothesized that race and proximity to high crime neighborhoods would negatively influence the perception of EFIC and decrease willingness to participate.
**Methods**: As part of an EFIC community consultation process, trauma patients, their families and community members living within the city limits of Philadelphia were asked to rank statements regarding EFIC and willingness to participate in emergency research using a 5-point Likert-type scale. Higher total scores reflected a more positive attitude regarding EFIC (range, 6-30; neutral = 18) and willingness (range, 23-115, neutral = 69). Subject zip code information was utilized to calculate proximity to the top 5 most violent zip codes in Philadelphia. The association between violence proximity and scores, race, group, and mechanism of injury was evaluated using linear regression modeling, t-test, Kruskal-Wallis and omnibus tests where appropriate ($p<0.05$).
**Results**: A total of 179 subjects participated and included trauma patients (n=99), their families (n=33) and community members (n=47). Overall, the cohort reported high EFIC perception and willingness to participate scores (median 24, IQR 13-30 and median 89, IQR 52-115 respectively). Community members were more likely to live in a distribution near violent neighborhoods than either patients or their families ($p=0.023$), but median proximity to these neighborhoods was no different between patients, their families and community members. Proximity to high crime areas correlated with violent mechanism of injury ($p=0.021$), but was not associated with race, the perception of EFIC or the willingness to participate in emergency research.
**Conclusion**: Proximity to high crime zip codes does not appear to decrease willingness or worsen the perception of EFIC. While researchers have been concerned that consulting high crime and urban communities could be a roadblock to implementing EFIC in emergency research, our data suggest that this may not be the case. Given the importance of EFIC research in the care of injured patients, this data should embolden future research pursuits.

**Background**

Accidental and violence-related injuries are two of the most significant causes of preventable death and disability in the United States (1). In fact, unintentional injury resulted in over 29 million visits to the emergency department in 2011 and is the leading cause of death in those under the age of 45 years old (1). In order to improve and optimize care of the injured, early interventions must be critically evaluated and prospectively studied. One of the major challenges associated with conducting trauma research, however, is that of obtaining informed consent from critically ill patients (2). Recognizing the need to improve emergency research while continuing to protect patient autonomy, the Food and Drug Administration (FDA) and the Department of Health and Human Services established guidelines for Exception from Informed Consent (EFIC) for emergency research in 1996 (3). Under these strict guidelines, emergency research may be conducted in the absence of explicit consent provided the subjects have a life-threatening condition, the research holds the prospect of direct benefit, and consent is not feasible. Additionally, the FDA guidelines require that a community consultation be conducted prior to initiation of the trial (4).

Currently there are no standards regarding the conduct of a "community consultation" process and the approach has varied widely in the literature (5-14). In many cases, the consultation has included a "community" survey documenting factors that influence both attitudes and willingness to participate in emergency research. While many community consultation studies have demonstrated a generally positive view toward EFIC and a proclivity toward consent, factors such as gender, race, socioeconomic status and educational level may contribute to lower rates of willingness (5, 7, 14-16). Willingness to participate may also be influenced by exposure to violence (17). Given the burden of life-threatening trauma and the

unique demographics associated with urban trauma centers, it is imperative that we understand this "community's" perception of EFIC research and develop guidelines to assist researchers and institutional review boards in the process of community consultation. We hypothesized that race, socioeconomic status and closer proximity to violence would make urban trauma patients, their families and community members less willing to participate in, and more skeptical of, EFIC research.

**Methods**

As a component of an IRB-approved community consultation for the AVERT Shock Trial (a trial investigating the use of vasopressin during the resuscitation of hemorrhagic shock) (18) voluntary, in-person interviews were conducted. A convenience sample of trauma patients, their families, and community members were approached in one of three settings: in-hospital prior to discharge, clinic follow-up visit, or at a community focus group. Discharge-ready patients and their family members who were mentally and physically capable of completing a 20 minute interview were approached daily between the hours of 9 am and 9 pm. Patients and family members who did not participate while hospitalized were invited to participate during their first outpatient appointment. Community members were invited to participate in a one of six 2-hour structured focus groups sponsored by a Baptist church, a mosque, three community organizations, and a recreational center located in the West Philadelphia neighborhood. After obtaining informed consent, participants were asked by trained research staff, including a research coordinator, research assistants and research physicians, to respond to a 42-item modified Clinical Research Involvement Scale (CRIS). The CRIS is a validated and reliable instrument designed to measure community attitudes toward participation in biomedical research studies (19). The items included demographic, dichotomous (yes/no) and 5-point Likert scale

ranked statements regarding attitudes toward EFIC and general willingness to participate in emergency research (SDC 1). Ranked responses were reverse coded where appropriate such that higher scores reflected a more positive attitude regarding EFIC.

The Avert ATTITUDE score was calculated from the sum of answers to six Likert-scale attitude questions (range 6-30; neutral = 18) and reflected attitude toward enrollment in the AVERT Shock Trial under EFIC. The WILLINGNESS score was calculated from the sum of answers to 23 Likert-scale willingness questions (range 23-115, neutral = 69) and reflected general attitude toward emergency research. Cronbach's alpha measure of internal consistency was then calculated for the ATTIUDE and WILLINGNESS scores and was found to be acceptable.

Subjects who lived in a zip code outside the City of Philadelphia and those with incomplete records were eliminated from analysis. Subject zip codes were used to estimate median income using 2011 Census Bureau data as a marker for socioeconomic status (20, 21). Subject zip codes were also used to calculate proximity to the 5 most violent zip codes in Philadelphia. These "violent hotspots" were identified using data provided by the Philadelphia Police Department to the University of Pennsylvania Cartographic Modeling Laboratory (22). These hotspots were defined as the five Philadelphia zip codes with the highest aggravated assault rate per 1,000 (Figure 1) (22). The shortest distance between subject zip code and violent hotspot zip codes was used in "proximity to violence" analysis.

Data were analyzed using SPSS (version 20.0, SPSS Inc., Chicago, IL). Multivariable linear regression, Spearman's correlation and Kruskal-Wallis tests ($p<0.05$) were used to evaluate relationships between role as patient, family member or community member, race, gender, age, estimated socioeconomic status, mechanism of injury (for patient and family

members), proximity to violence, attitudes toward EFIC in the context of the Avert Shock trial and willingness to participate in emergency research.

**Results**

179 subjects including trauma patients (n=99), families (n=33) and community members (n=47) were included in analysis. There was an overall response rate of 92%. Respondents were primarily African-American (83%), evenly split between male (54%) and female (46%) and distributed across age ranges (Table 1). Respondents lived an average of 2.74 (0-10.2) miles from the nearest violent hotspot and 3.7 (0-15.7) miles from our Level 1 Trauma Center with an estimated median income of $32,313 (range $14,586 to $93,222) (20). Respondents lived in 30 of the 49 zip codes found in Philadelphia.

Overall, participants were supportive of EFIC as reflected by Avert ATTITUDE scores (median=24, IQR 21-25) and WILLINGNESS to participate scores (median=89, IQR 82-95, Table 2). Importantly, median participant scores were well above neutral rankings; a score of 18 for Avert ATTITUDE and 69 for WILLINGNESS. There was no correlation between Avert ATTITUDE or WILLINGNESS scores and race, gender, age, estimated median income or status as inpatient or outpatient. A correlation was found between Avert ATTITUDE score and role, with community members having a more positive attitude toward EFIC than families or patients (median 25, 24, 23, $p<0.01$, Table 2). However, there was no correlation between WILLINGNESS scores and role.

"Proximity to violence" did not correlate with perception of EFIC, willingness to participate in emergency research or violent mechanism of injury, but was associated with African-American race ($p=0.03$) and socioeconomic status ($p<0.01$) (Table 3). Additionally, there was no correlation found between living within a "violent hotspot" and perception of EFIC

in the context of the Avert trial or willingness to participate in emergency research. Similarly, no correlation was detected between having experienced, or known someone who had experienced, a significant trauma resulting in blood loss and Avert ATTITUDE or general WILLINGNESS scores. However, a correlation was found between mechanism of injury and Avert ATTITUDE score, with patients or families of patients injured by a non-violent mechanism having a more positive attitude toward EFIC than those injured by assault, gunshot or stab wound ($p<0.01$) (Table 2). In contrast, there was no correlation found between mechanism of injury and WILLINGNESS to participate in emergency research.

**Discussion**

The community consultation process is a central and valuable requirement for conducting emergency research under EFIC (3, 4). Through our community consultation process, we sought to further understand the factors that influence attitudes toward EFIC in the context of the Avert Shock trial among urban trauma patients, families and community members by engaging with both our geographic and at-risk patient communities. In contrast to previous reports, we found that gender, race, and estimated socioeconomic status did not influence views on emergency research. Moreover, we found that living in or near a violent hotspot had no influence on attitudes toward the Avert Shock Trial or general willingness to participate in emergency research using EFIC. Collectively, these findings should embolden researchers and Institutional Review Boards to partner with at risk communities in order to conduct emergency research.

Since people living closest to areas of concentrated violence are more likely to be the victims of violent injury (21) we anticipated an association between proximity to violence and violent mechanism of injury. In the City of Philadelphia, the rate of aggravated assault per 1,000 residents ranges from 0.64 in the safest zip code to 10.79 in the most violent (22). Among

respondents living within one of the 5 most violent zip codes, 51.6% had either known someone or had themselves been the victim of a traumatic injury requiring blood product or fluid resuscitation. In contrast, only 38.5% of respondents living outside these violent hotspots had a similar experience (p=0.05).

Proximity to violence, however, had no influence on the perception of emergency research in our study. Using proximity as a corollary for exposure to violence, we theorized that those living closer to violent hotspots would be more likely to develop collateral consequences of chronic direct or indirect exposure to trauma (23). Stress theory suggests that exposure to community violence closely correlates with emotional, social and behavioral maladaptation, including anxiety, PTSD, and social and educational disengagement (24). In a study using data representing over 20,000 adolescents from the National Longitudinal Study of Adolescent Health, Warner, et al found that violent victimization among youth was associated with decreased survival expectation, placing them at increased risk for social disengagement (25). As such, we hypothesized the potential presence of these maladaptive influences would make respondents less willing to participate in emergency research. In the course of this community consultation, however, we found no direct correlation between proximity to violence and willingness to participate in emergency research. While it is possible that our respondents were not negatively influenced by proximity to violence, it is also possible that the community consultation process minimized the effect of these influences on the respondent's attitudes and willingness. The concept that education and community involvement can improve diverse participation in clinical trials is critical to emergency research, and was the central theme of a recent national meeting on the topic (26).

Contrary to our hypothesis, community members living the closest to violent hotspots actually demonstrated a positive attitude toward EFIC and a trend toward increased willingness (Table 2). In our study, community members lived an average of 1.95 miles from the nearest violent hotspot. In fact, 35% of community members surveyed actually lived within a violent hotspot and, therefore, theoretically had the highest exposure to violence. Perhaps this increased exposure to, as well as the direct community consequences of violence, made community members feel a stronger responsibility to find effective solutions for the problem. Hill, et al found this to be the case in a study investigating the relationship between exposure to violence and coping strategies among African-American mothers, where activism was identified as a commonly employed strategy (27).

Violent mechanism of injury, however, represents a direct exposure to violence and may acutely influence a subject's attitude and willingness to participate in emergency research. We have previously reported a correlation between violent injury mechanism and decreased support of EFIC in a more heterogeneous group of respondents (17). We have built on this prior work and have identified these same trends in our urban resident cohort. Although violent mechanism of injury negatively influenced attitudes toward EFIC in the context of the Avert Shock Trial, it did not diminish the general willingness to participate in emergency research (Table 2). This lack of association reinforces the assertion that our urban "community's" exposure to violence should not negatively bias our willingness to partner with those most at risk for violent injury.

That being said, there is an undeniable history of unethical medical research conducted in disenfranchised communities; and it is not surprising that race and socioeconomic status have been previously shown to correlate with mistrust of the medical establishment. In particular, the infamous Tuskegee Syphilis Experiment still influences opinion about research today (28, 29).

As a result, African-American race has been independently associated with distrust of medical investigators, even after controlling for social class (28). Moreover, African American race appears to significantly influence the willingness to participate in EFIC research (30). When presented with a theoretical study, Baren et al found that African American parents were significantly less likely to consent to emergency research than Caucasian parents (5). Given that the two most impoverished zip codes are also violent hotspots in which the majority of residents are African-American (Figures 2 and 3), we were surprised to discover that our study demonstrated no direct correlation between race and willingness to participate in emergency research. Similarly, socioeconomic status did not correlate with attitude toward or willingness to consent to emergency research.

Finally, gender has been previously implicated as a factor influencing willingness to participate in emergency research; a correlation that we did not observe (31, 32). Although 70% of our trauma patient population is male, half of the total respondents in our study were female family members and community meeting participants (11, 33). Female family members may be more likely to visit patients in-hospital or accompany them to outpatient appointments; or females may be more likely to voluntary as survey participants. Regardless, if one goal of the community consultation process is to generate discourse with the individuals who will be providing emergency consent, it is appropriate for females to be equally represented because mothers frequently function as legally authorized representatives in our trauma population (unpublished data).

So, why is there discordance between our findings and those of many prior well-conducted studies (5, 7, 31)? The answer may lie in the approach we took to conduct our community consultation. Our process included a significant educational component aimed at

building understanding and trust between respondent and researcher, an essential component of the relationship required for successful EFIC investigations (7, 11, 33, 34). Specifically, each subject completed the survey in the context of either a semi-structured interview while in-hospital or at clinic, or following an hour long community- based focus group. As Thomas found: "Engaging in dialogue with at-risk groups often empowers them to create effective solutions for addressing concerns." (35) In this study, we engaged with an urban community at risk for inclusion in a trial investigating a novel therapy for hemorrhagic shock. Although at the outset of this investigation we theorized that race, socioeconomic status and exposure to violence would lead to lower levels of willingness to collaborate with researchers, we found this not to be the case. We believe our positive findings resulted from a community consultation process that engaged with and educated the geographic and at-risk community. By understanding the potential benefits of emergency research in the context of one of the community's pervasive public health issues, we believe respondents were able to look beyond underlying mistrust of the medical establishment toward a more considered opinion about trauma research.

Additionally, though previous studies have found associations between income and consent decisions in EFIC trials, these trials relied on either read survey tools or those administered during acute care in the emergency department (5, 7). In contrast, our community consultation process included significant one-on-one education about the need for emergency research, the process of EFIC research, and details regarding the upcoming AVERT Shock trial. While this process is certainly more resource-intensive, it may serve to overcome the well-documented issue of illiteracy for individuals engaged in community consultation (36-38) while minimizing the impact of socioeconomic status (7, 14) and providing an opportunity for trust to develop between researcher and subject.

There are a number of limitations to this study. Performance of a community consultation in the context of a widely supported trial certainly could influence attitudes toward EFIC. Additionally, there is a selection bias for patients and families, as we collected a convenience sample of those who were well enough to participate in a 20 minutes interview (39). This would exclude the patients and families of patients who were acutely ill or who died as a result of their injury. These patients and families may not have been as supportive of emergency research as those who were well enough to be discharged from the hospital. Voluntary convenience sampling could also lead to selection bias (39, 40). Patients and families willing to participate in the interviews may have been those generally more in support of research. Similarly members of the community who were willing to participate in focus groups may have been generally more in support of research. Members of the community with mistrust of the medical establishment and more negative attitudes toward research, researchers and medicine in general, could have been either under- or over-represented. While the responses of our community members were statistically more positive than those of our patients and family members, all groups attitude and willingness scores were well above neutrality. Although is true that when people are informed of an EFIC study they are more likely to have a positive attitude (41), one of the mandates of a community consultation is to inform the community and solicit their educated advice and recommendations regarding the proposed research. In addition, estimation of proximity to violence was based on zip code data of the respondent and the zip codes of violent hotspots. This could lead to either over or under-estimation of the subject's actual proximity to violent hotspots. The survey response rate for actual income was less than 20%, therefore we estimated income based on the median income for a zip code. It is certainly possible that the median income for the respondent's zip code could misrepresent their actual

income. Lastly, this is a retrospective post hoc analysis and therefore the data is not powered to prevent a type 2 error.

Based on our data, we found no correlation between race, socioeconomic status or proximity to violence and willingness to participate in EFIC research. Given this lack of correlation, researchers should partner with at-risk communities to conduct EFIC studies without concern that the consultation will be negatively biased. Moreover, because EFIC research is absolutely essential in order to develop life-saving treatments, our research can also serve as part of the growing body of literature providing guidance for Institutional Review Boards as they navigate the community consultation process (42). Although there remains on-going and valid concern regarding the most effective method for engaging the community, we believe that community education and thoughtful partnerships with those most at-risk are investments worth making. It is clear that the time has come for collaboration between at-risk communities and researchers in the pursuit of better emergency care.

**Author Contribution**

Z.M., E.G., and C.A.S designed this study.

C.A.S. contributed to data collection.

Z.M., E.G., and B.P.S. performed data analysis.

Z.M., E.G., B.P.S., and C.A.S performed data interpretation.

Z.M., E.G., and C.A.S prepared the article.

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Legend

SDC 1 – Modified Clinical Research Involvement Scale Attitude and Willingness Items

Table 1 – Demographics of the Study Population

Table 2 – Univariate Analysis of AVERT Attitude and EFIC Willingness Scores

Table 3 – Proximity to Violence or Socioeconomic Status Correlations

Figure 1 – Aggravated Assault rate/1,000 population by Philadelphia zip code

Figure 2 – Percentage of residents 200% below poverty line by Philadelphia zip code

Figure 3 – Percentage of African-American residents by Philadelphia zip code

Description

Table 1 – Spearman's correlation was used to evaluate relationships between variables. Pairwise comparison was then used to further evaluate significance.

Table 2 – Kruskal-Wallis test used to evaluate for significance of variables between groups. Pairwise comparison was then used to further evaluate significance.

Table 3 – Spearman's correlation was used to evaluate relationships between two variables.